EXAMINER'S AMENDMENT

Election/Restrictions

Because the elected invention was drawn to a method of making, the products claimed being withdrawn from consideration and not eligible for rejoinder under In re Ochiai, Applicant has agreed to the cancellation of all withdrawn product claims. **The restriction requirement as set forth in the Office action mailed on 9/25/06 is hereby withdrawn**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Thomas Finetti, Applicant's Representative, on 9/29/09.

IN THE CLAIMS

Claims 20-25 and 29-45 have been cancelled without prejudice.

Reasons for Allowance

The following is an examiner's statement of reasons for allowance:

A method for synthesis of a KPV tripeptide diamide derivative of formula (I), comprising the steps as claimed, was not found to be reasonably taught or suggested by the prior art of record. As Applicant points out on page 13-14 of the response of 6/23/09, the claimed steps provided for unexpected results in increased yield of the KPV tripeptide diamide derivative of formula (I):

> "The Examiner, however, believes the disclosures in the application at paragraphs [0051] and [0052] are also taken from Eberle and relies on them to establish a prima facie case of obviousness. Office Action, pages 3-4, 6. This is not the case. Rather, paragraphs [0051] and [0052] are statements directed to the claimed invention, and serve to provide a summary of the claimed methods. These paragraphs provide the following:
>
> It is shown, according to the invention, that a particular combination of synthesis steps and the use of a particular combination of protective groups make it possible to prepare KPV tripeptide diamide derivates, or a salt of such compounds, in a solution synthesis method with a final yield much higher than the yield obtained with the known state of the art methods, and such a method does not require any final purification step, such as for example via ion exchange chromatography.
>
> It has been shown that an appropriate selection of the protective groups, the reagents to be used and the reaction sequence makes it possible to increase the yield, in a solution synthesis, from 33% (Eberle et al., 1975) to more than 70% in the case of Ac-Lys-Pro-Val-NH2.
>
> Application, para's [0051], [0052], emphasis supplied. There can be no mistake that these passages refer to the methods of the claimed invention, and provide an overview of the procedures used and results obtained. This is especially true in view of the underlined passages which specifically compare the present invention with the known art, and Eberle in particular.
>
> More importantly, these passages do not teach the ordering of reaction sequences or the selection of protective groups. Nor do they provide a suggestion that the methods of Eberle can increase reaction yield.
>
> [ ]

> When properly considered, Eberle teaches a convergent synthesis of a KPV tripeptide, where two starting materials, namely a Pro-Val-NH2 dipeptide and a Boc-Lys(MSOC)-OH compound, are first prepared separately. Id. The two compounds are then coupled together followed by removal of the -Boc protecting group, acetylation on the Lys residue, and removal of the –MSOC group. Id.
>
> In contrast, the claimed invention is directed to a linear synthesis of Ac-KPV-NH2, i.e. building the KPV backbone, starting by reacting lysine with proline, and adding or removing protecting groups and reagents when necessary to achieve the appropriate functionality of the final KPV tripeptide.
>
> Eberle neither teaches such a linear synthesis nor the unique protection/deprotection scheme of the claimed invention, used in this completely different synthetic scheme. There simply is no disclosure in Eberle to teach one skilled in the art to synthesize a functionalized KPV tripeptide through a linear synthesis, let alone with increased yields.
>
> Nor do the secondary references cure this deficiency. [ ]"

For the reasons of record, Applicant has established an advancement in the art of preparing increased yields of KPV tripeptide diamide, based on his findings using the method/steps presently claimed. The claimed invention is hereby allowed.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Claims 1-11, 15-19, 27, and 46 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAURY AUDET whose telephone number is (571)272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 10/26/2009

/Maury Audet/
Examiner, Art Unit 1654
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